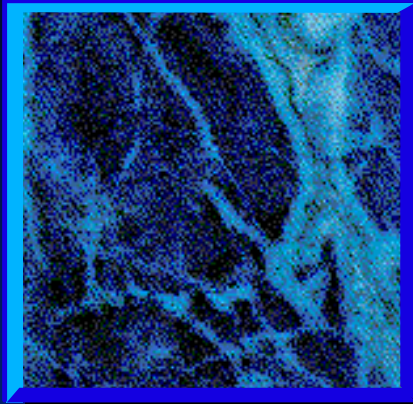
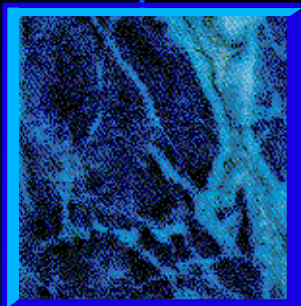


Animal TSEs in the United States: Surveillance and Response



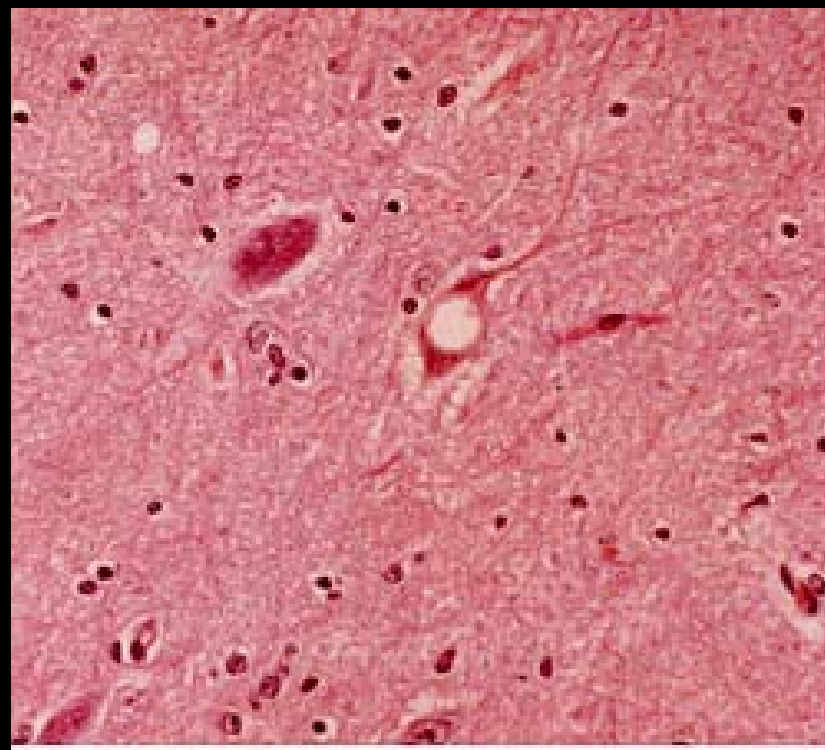
Linda A. Detwiler
Senior Staff Veterinarian
USDA, APHIS, VS

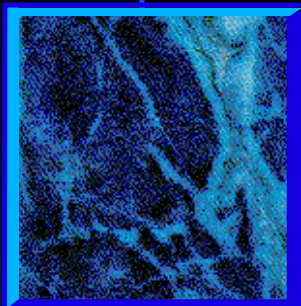




Transmissible Spongiform Encephalopathies

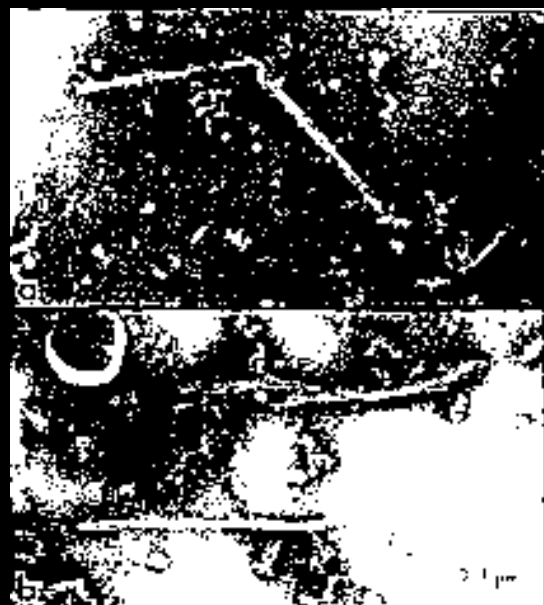
- prolonged incubation period
- progressive debilitating neurological illness
- pathological changes confined to CNS
- fatal

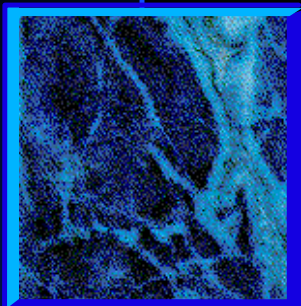




Transmissible Spongiform Encephalopathies

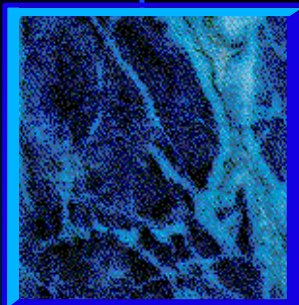
- Scrapie Associated Fibrils (SAF) - negative stain EM
- Transmissibility





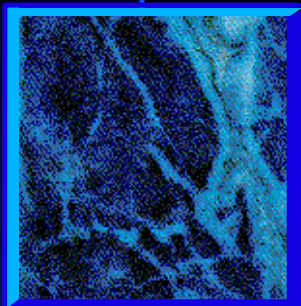
Transmissible Spongiform Encephalopathies: Etiology

- agent not fully characterized
- smaller than smallest known virus
- elicits no detectable immune or inflammatory response in the host
- resistant to most disinfectants and treatments which normally destroy nucleic acids



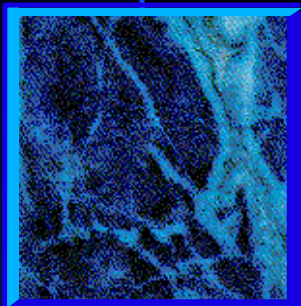
Etiology: Is the agent a Prion?





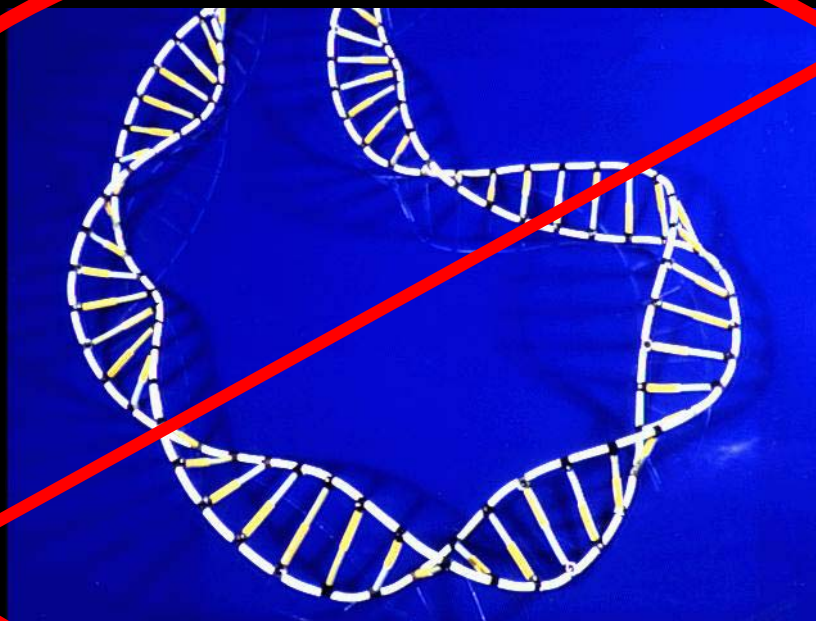
Etiology: Prion

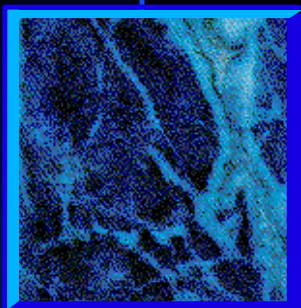
- host-coded normal cellular protein becomes partially protease resistant through post translational conformation change
- alpha helix to beta sheet



Etiology: Prion (*continued*)

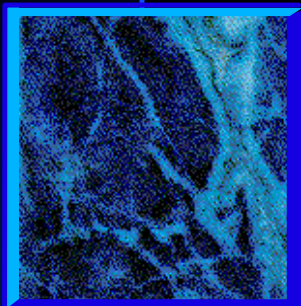
- no non-host component
- no nucleic acid





Transmissible Spongiform Encephalopathies: Agent Theories

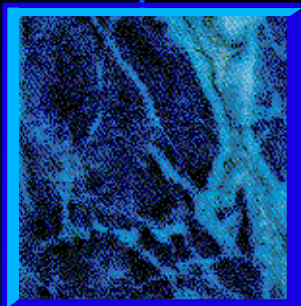
- **BUT** - created protein not infectious, PrP^{res} not always infectious; disease without PrP^{res}
- **VIRUS** - unconventional, unusual biochemical and biophysical properties
- **VIRINO** - host-derived protein coat coupled to a small noncoding regulatory nucleic acid



Transmissible Spongiform Encephalopathies: Human

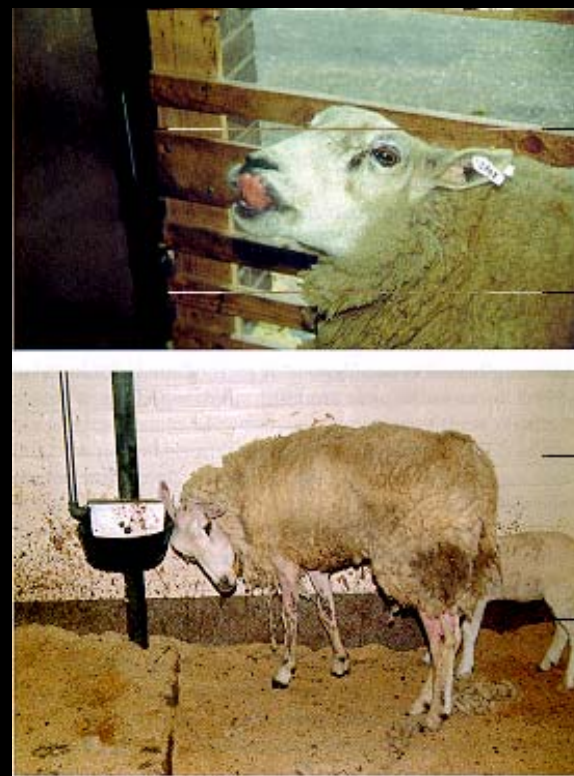
- Creutzfeldt-Jakob Disease (CJD)
- Gerstmann-Straussler-Scheinker syndrome (GSS)
- fatal familial insomnia (FFI)
- Kuru
- variant CJD (vCJD)

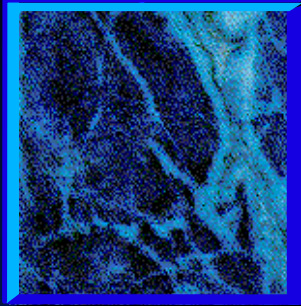




Transmissible Spongiform Encephalopathies: Scrapie

- Reported most sheep producing regions
- Known over 250 years
- Sheep, goats, moufflon

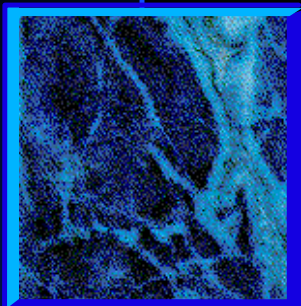




Transmissible Spongiform Encephalopathies: Chronic Wasting Disease

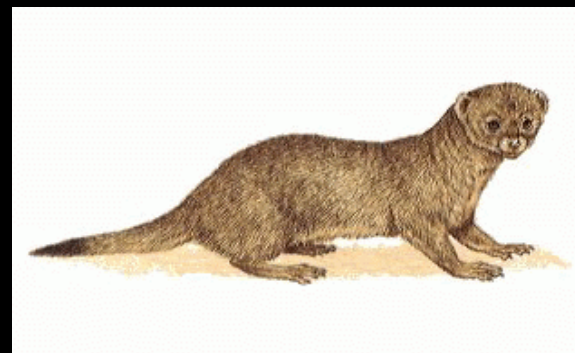
- First recognized as disease syndrome - 1967
- Colorado, Wyoming - endemic areas
- Free-ranging South Dakota, Wisconsin, Western Nebraska
- Farm raised elk - US and Canada

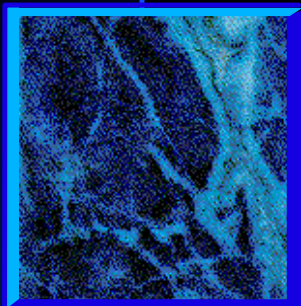




Transmissible Spongiform Encephalopathies: Transmissible Mink Encephalopathy

- Affects ranch raised mink
- First recognized in 1947
- Detected and documented in Canada, Finland, (East) Germany, Russia
- Associated with feed

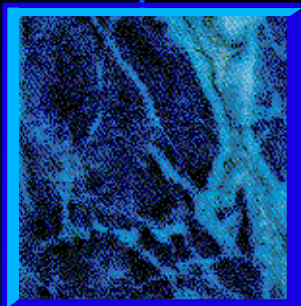




Transmissible Spongiform Encephalopathies: Animal

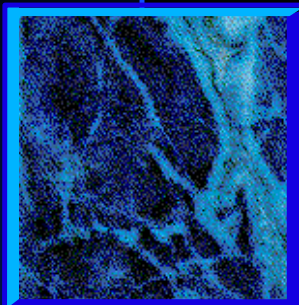
- Bovine Spongiform Encephalopathy
- Feline Spongiform Encephalopathy
- TSE of Exotic Ruminants





Animal TSEs in the US

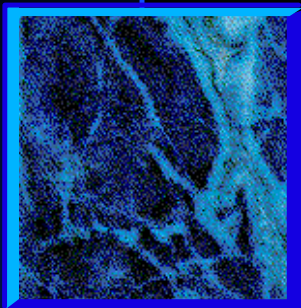
- Scrapie - endemic; control/eradication
- CWD - isolated? control/eradication
- TME - rare; last outbreak 1985
- BSE - not known to be present; prevention and surveillance



Chronic Wasting Disease - Definition

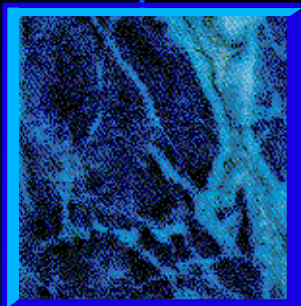
- Transmissible spongiform encephalopathy of adult deer and elk characterized by progressive weight loss and eventual death





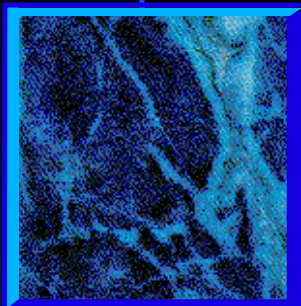
Cervid Species Affected

- Rocky Mountain Elk
- Mule Deer
- Black-tailed Deer
- White-tailed Deer
- Hybrid Deer



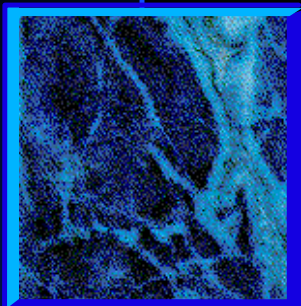
Chronic Wasting Disease - Distribution

- Cases in research facilities in Colorado and Wyoming
- Cases in free ranging animals in northeastern, northcentral Colorado, southeastern Wyoming, western Nebraska, South Dakota, Wisconsin
- Elk cases in captive herds (SD, NE, OK, CO, MT, KS)



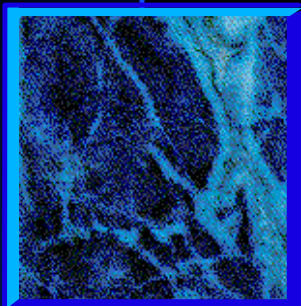
Chronic Wasting Disease - Distribution (*continued*)

- Cases in Zoological Parks and captive elk herds - Canada
- Prevalence in affected private elk herds varies from $<1\%$ to $> 30\%$ - under investigation



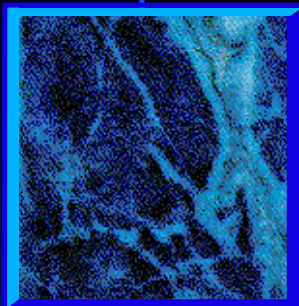
Chronic Wasting Disease - Distribution

- Hunter harvest cervid surveillance -1983
- Thousands cervids tested North America
- specific management units (endemic area)
estimated prevalence - 1-15% in mule deer and white-tailed deer ; <1% in elk
- In surrounding wildlife management units - estimated prevalence in deer and elk is <1%.



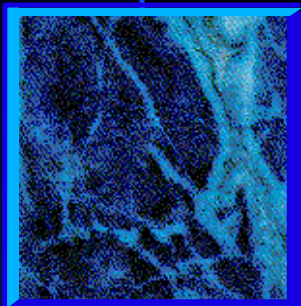
Chronic Wasting Disease - Epidemiology

- Origin, mode of transmission, and time from infection to shedding of organism and clinical disease are unknown
- Probably lateral transmission, possibly maternal
- Approximately 90% of mule deer held in one research facility developed CWD in one 12 yr period



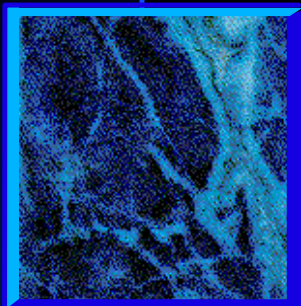
Chronic Wasting Disease - Epidemiology (*continued*)

- 17% of captive elk held in one "contaminated" facility developed CWD over an 11 year period
- Current Research



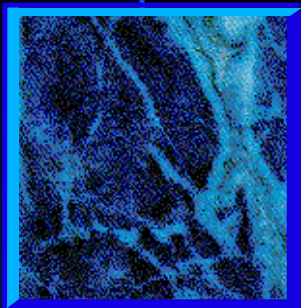
Chronic Wasting Disease - Clinical Signs

- Chronic wasting condition - continues to eat grain, hay consumption decreases
- Behavioral Changes - decreased interaction with herdmates, listlessness, repetitive walking, nervousness, hyperexcitability, hyperesthesia
- Excessive salivation/grinding teeth
- PU/PD
- Progressive and fatal



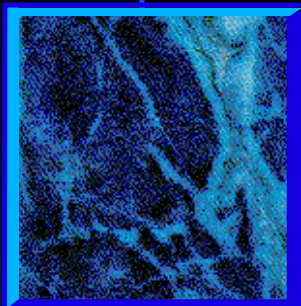
CWD - Distribution of Infectivity

- Central Nervous System
- Lymphoreticular System
- Ongoing research



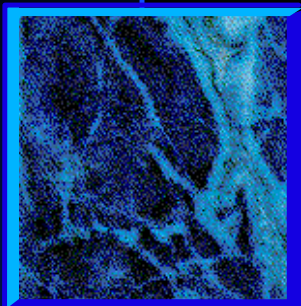
CWD - Pathology

- Emaciation - Lack of body fat, muscle atrophy
- Aspiration pneumonia
- Fluid rumen contents in deer
- Can be easy to miss!



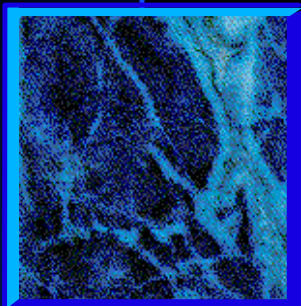
Chronic Wasting Disease: Research Needs

- Antemortem/Preclinical Diagnostic Tests
- Pathogenesis
- Epidemiology
- Cleaning and Disinfection Methods for Contaminated Premises



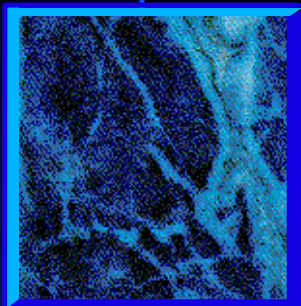
Chronic Wasting Disease: NAEBA Model Program

- Captive/farmed elk
- Adopted/Modified by states
- Fencing requirements
- Animal ID and herd inventory
- Surveillance of deaths over 16 months
- Herd status - years of surveillance
- Herd additions - same or greater status
- Positive - brain positive/NVSL confirmation



Chronic Wasting Disease: Future Direction

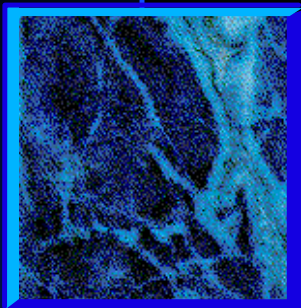
- **Continued Surveillance**
- **Continued Research Support**
- **Epidemiology**
- **National Herd Certification Plan and
Control Program Development**



Scrapie

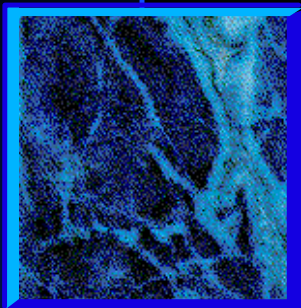
- endemic in the US
- first case 1947





Scrapie: Incubation

- 2 to 5 years
- US average - 3.5 yr (Wineland et al., 1998)
- can be shorter than 2 years (18 months)
- influenced by PrP genotype



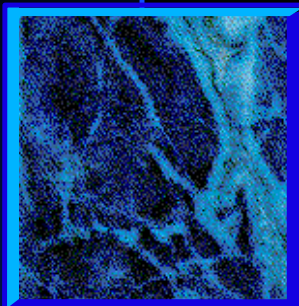
Scrapie Pathogenesis

Not all susceptible genotypes
develop disease -

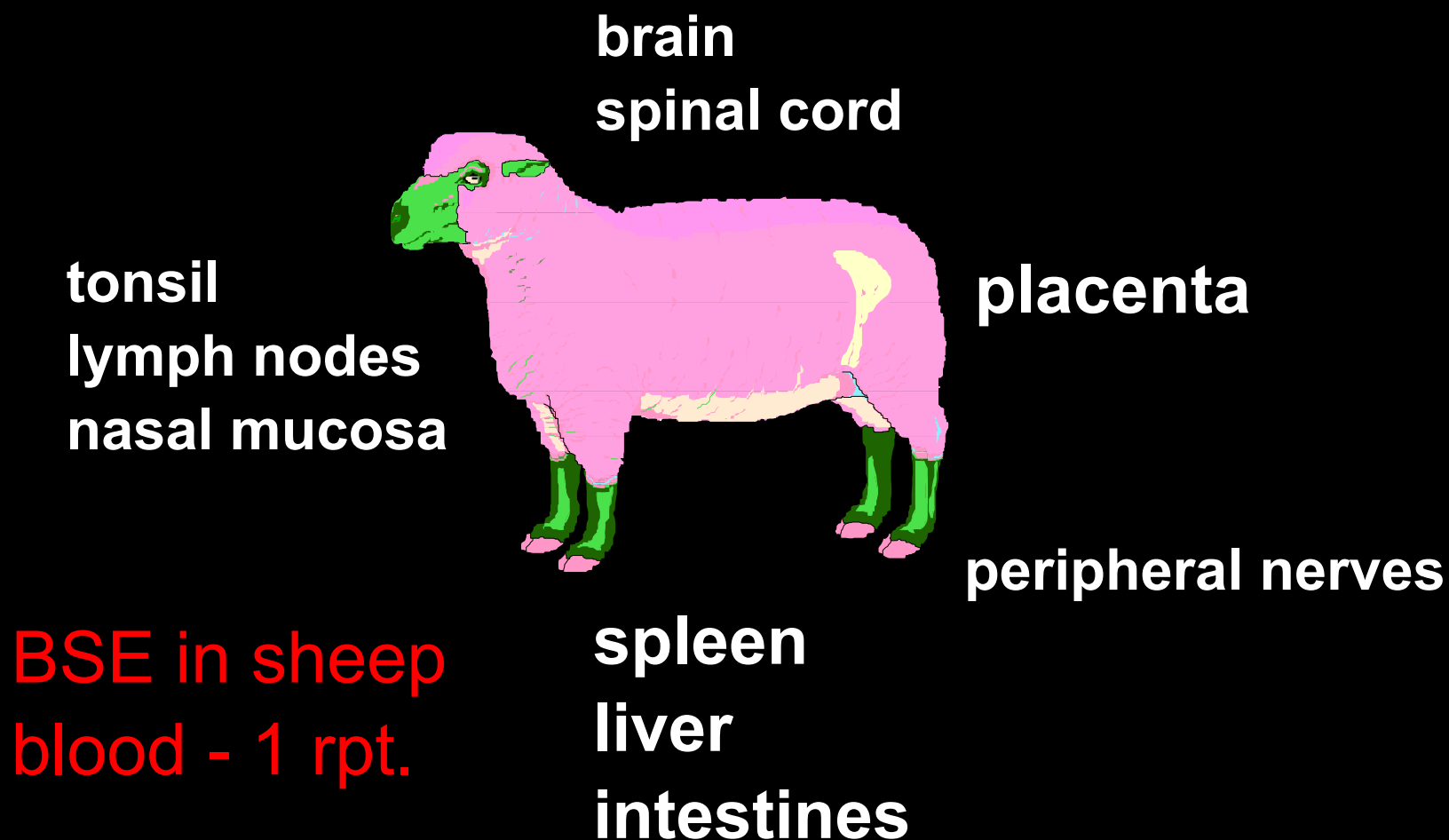
rumen contents

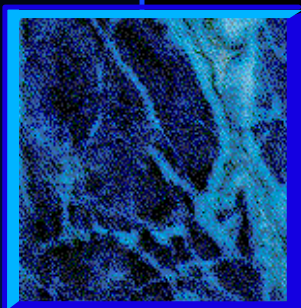
chance of exposure to receptors

maturity

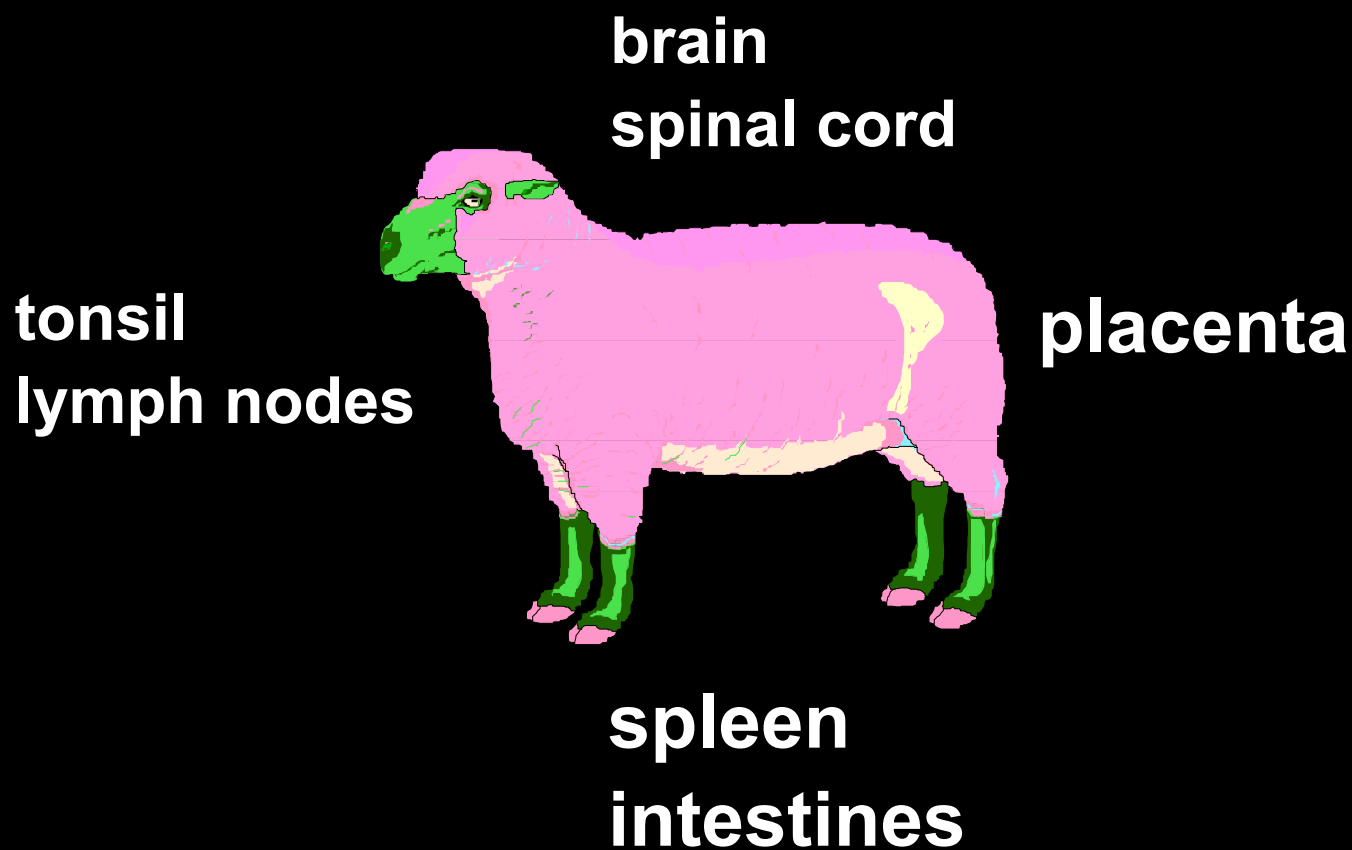


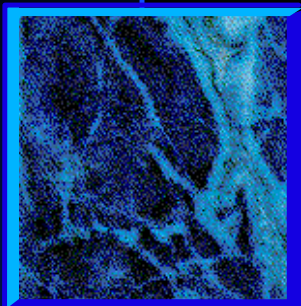
Scrapie: Distribution of Infectivity





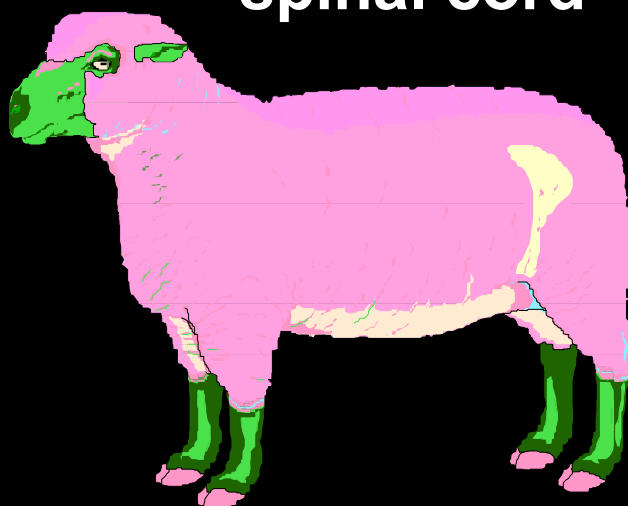
Scrapie: Distribution of PrP^{sc} (QQ)

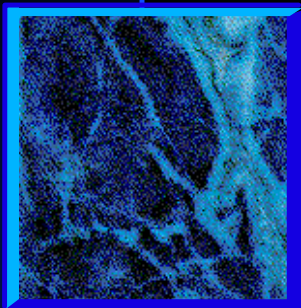




Scrapie: Distribution of PrP^{sc} (QR)

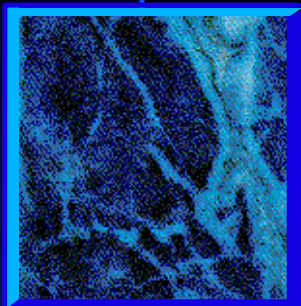
brain
spinal cord



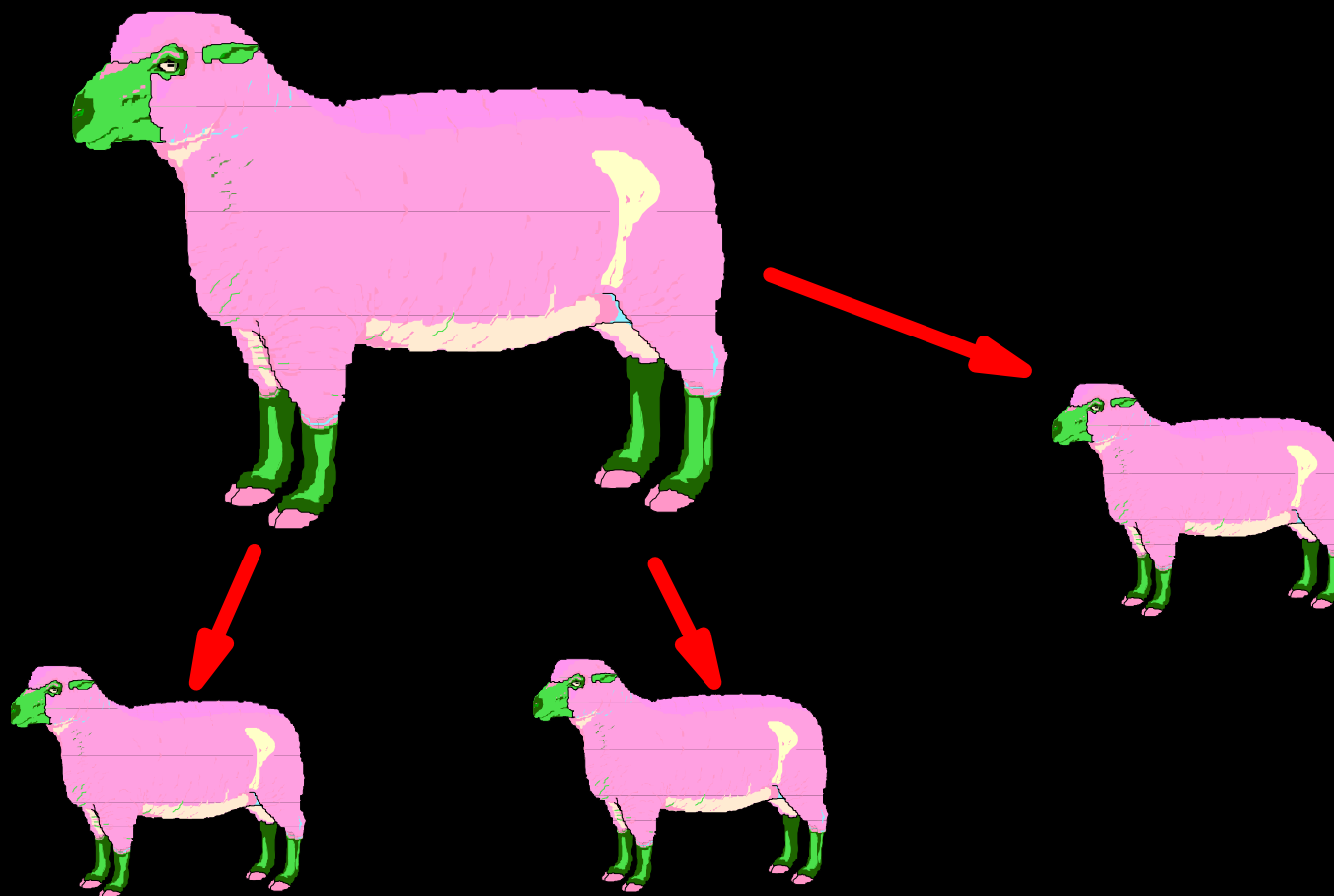


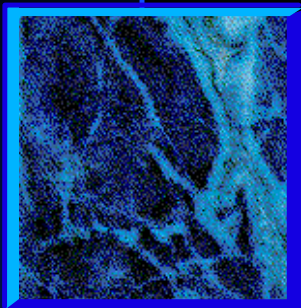
Scrapie Pathogenesis

- Oral route - primary
- Skin scarifications?
- Replication in Peyers Patches (2 months of age) then spread throughout GALT
- To CNS - ANS or blood????



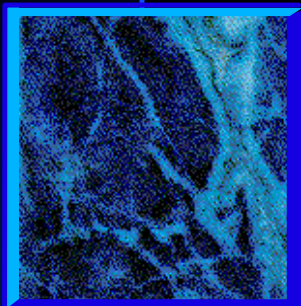
Scrapie: Transmission





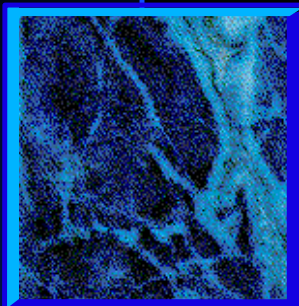
Scrapie Transmission

- 2 outbreaks by vaccines
- Louping Ill - UK
- M. agalactiae - Itlay



Scrapie Eradication/Control

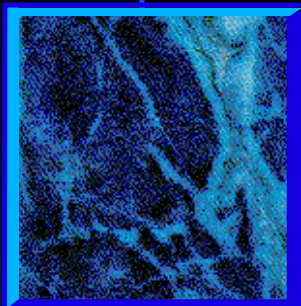
- Certification Program/Restrictions on Infected and Source Flocks
- Renewed Efforts
- New Funding (201 Action)
- Identification
- Consistency between States
- Test Validation
- Slaughterhouse surveillance



Transmissible Spongiform Encephalopathies: Family

- Long incubation diseases with no preclinical test
- Think - if I knew disease would be here tomorrow, what should I have done yesterday

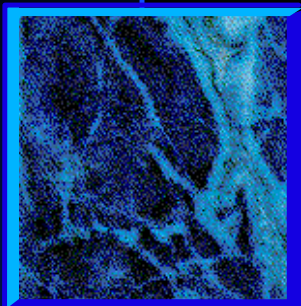




Transmissible Spongiform Encephalopathies: Animal

- Bovine Spongiform Encephalopathy (aka: mad cow disease)

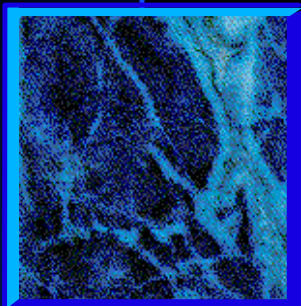




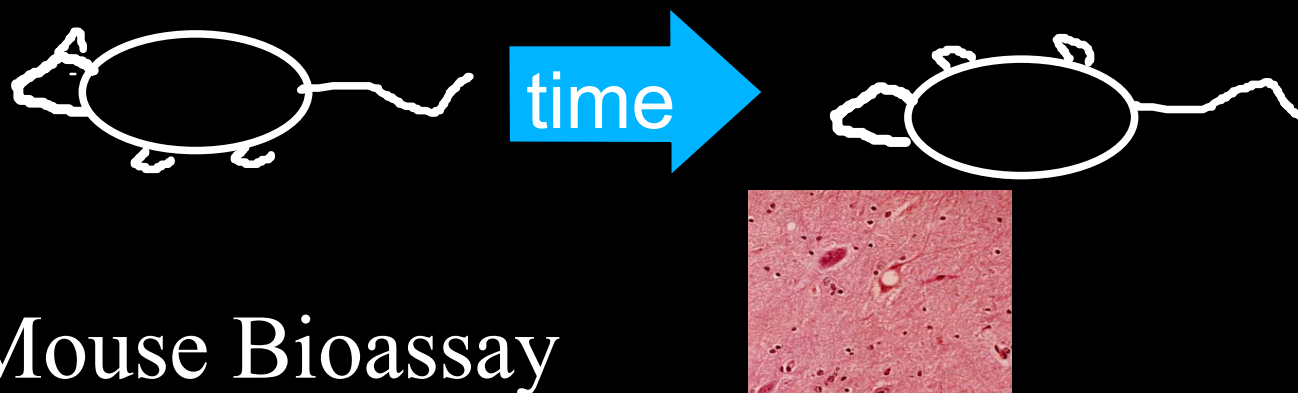
BSE: Other animal species

- Feline Spongiform Encephalopathy
- TSE of Exotic Ruminants



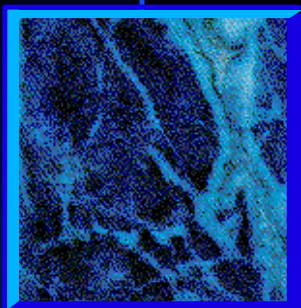


TSEs: Strain Typing



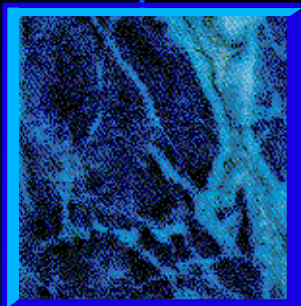
■ Mouse Bioassay

- ▲ length of incubation and lesion pattern
- ▲ 5 different breeds of mice
- ▲ Scrapie - numerous strains
- ▲ BSE/FSE/TSE in exotic ruminants/vCJD
- ▲ CWD - different from all others

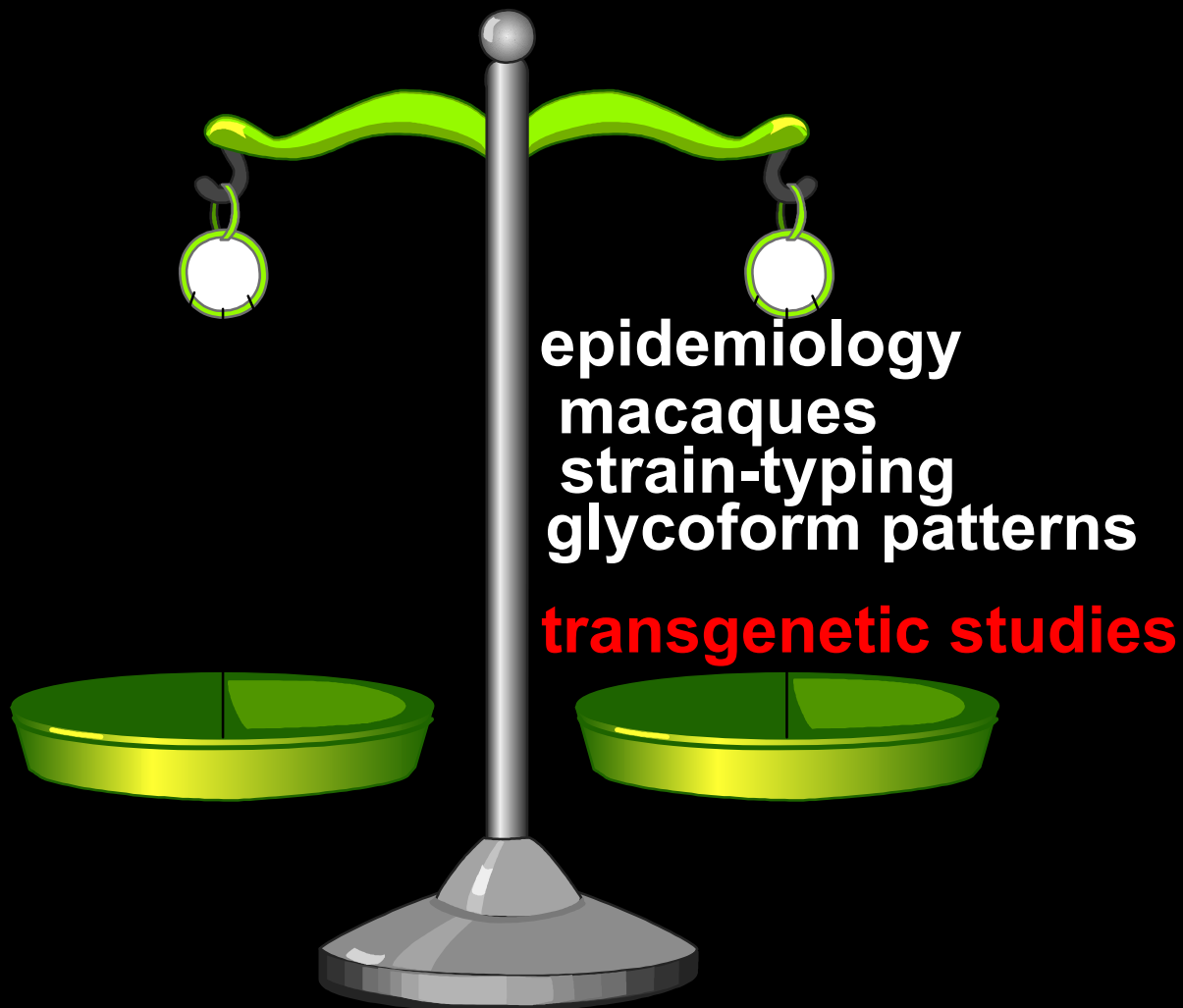


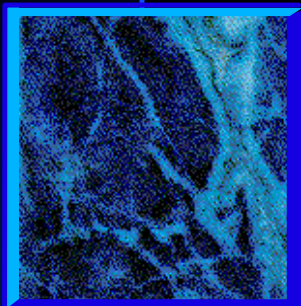
CJD vs. vCJD

- | | |
|------------------------------------|---|
| ■ sporadic, genetic, iatrogenic | ■ food contaminated with BSE infected CNS |
| ■ 55-75 yrs of age | ■ 28 yrs. median |
| ■ ≤ 6 mos clinical course | ■ avg 14 mos clinical course |
| ■ memory loss, myoclonus, dementia | ■ psychiatric followed by neuro |
| ■ no plaques in brain | ■ florid plaques |

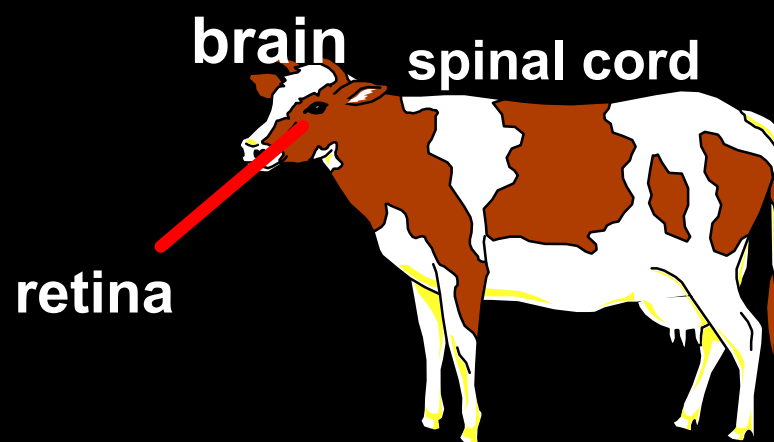


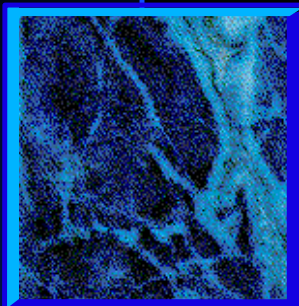
vCJD = BSE



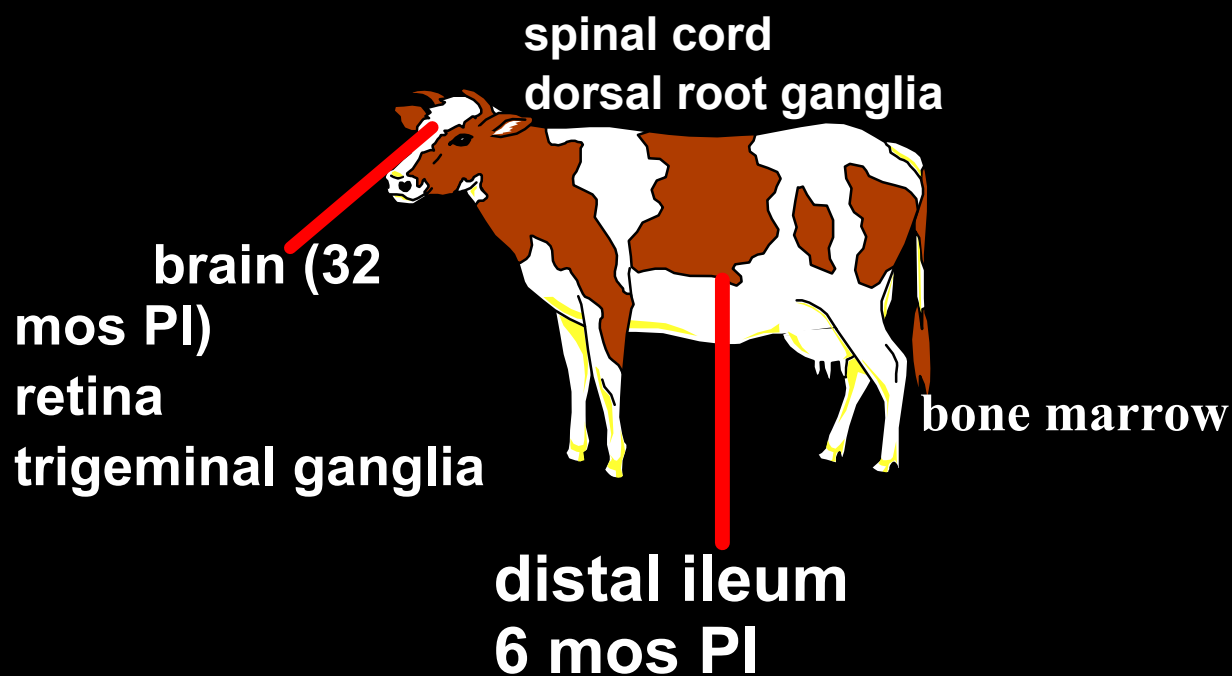


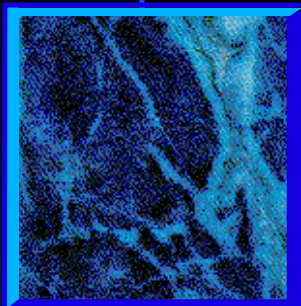
Distribution of Infectivity: Natural Cases





Distribution of Infectivity: Experimental

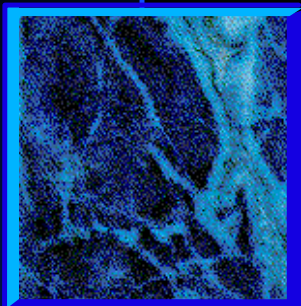




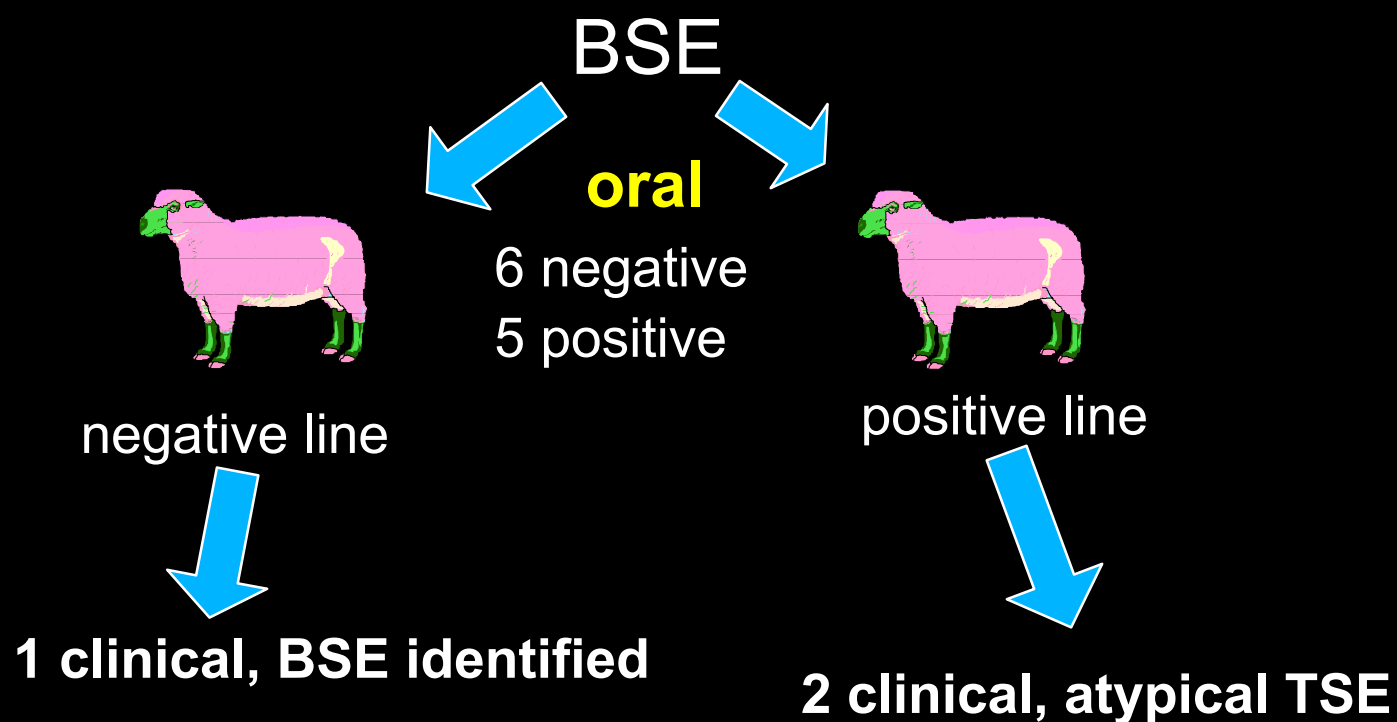
Transmission

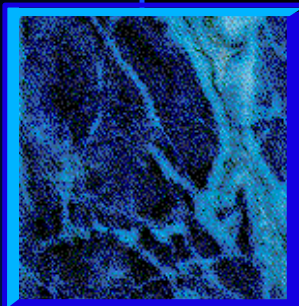


Cattle eats contaminated feed and gets sick in 3-6 years



BSE in Sheep: Research (Foster et. al.)

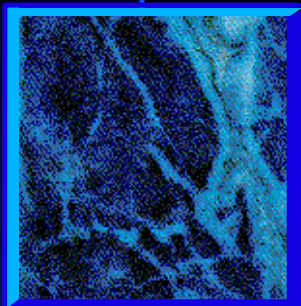




BSE in Sheep: Research

- Like scrapie - clinically, histologically, other tests
- differentiate mouse bioassay
- Spread like scrapie?

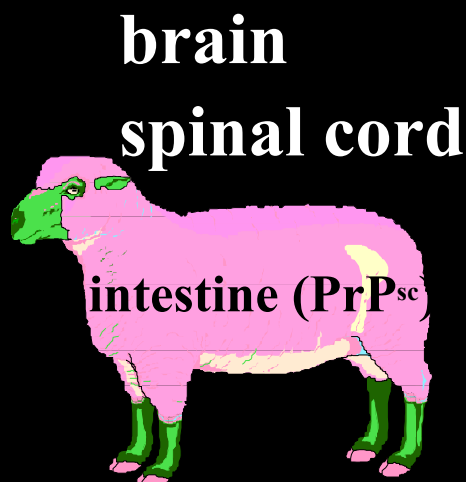




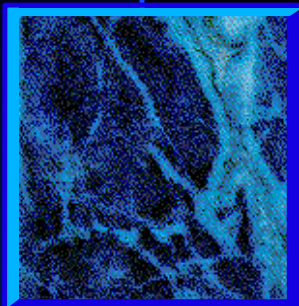
BSE in Sheep: Research

Distribution of Infectivity

**blood-1
report
(Houston
et al.,
2000)**

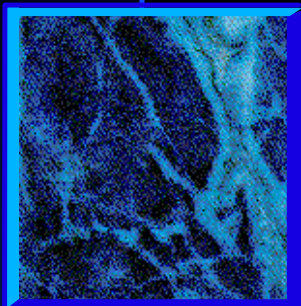


**spleen
(Foster
et al.,
1996)**

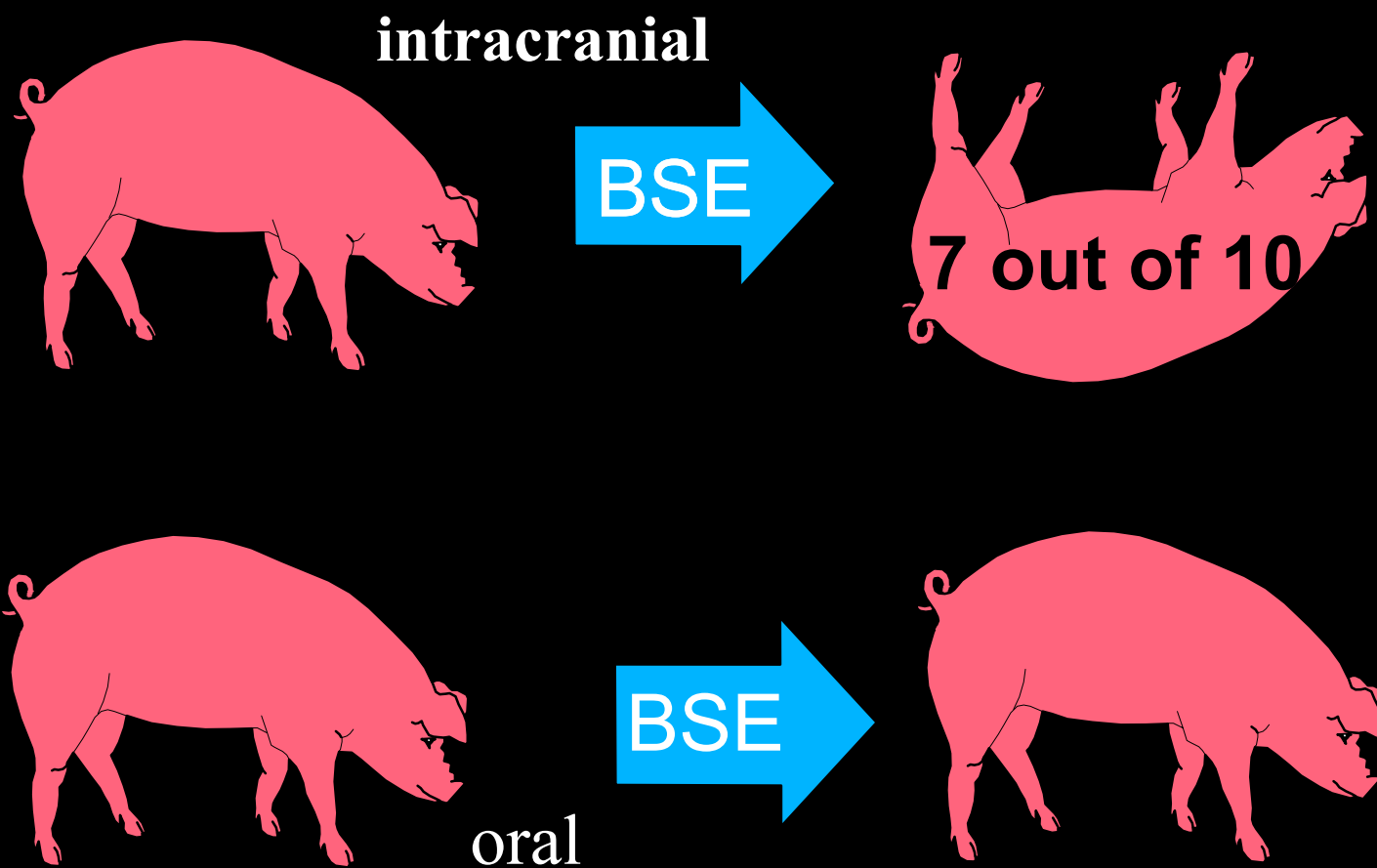


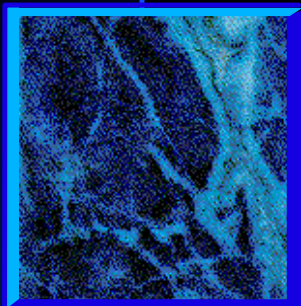
BSE in Sheep: European Situation

- Exposure to contaminated MBM
- Surveillance for natural cases
- Must differentiate from scrapie - mouse bioassay system (2-3 yrs)
- None to date - limited number assessed
- Public Health Protection - SRM ban on sheep and goat tissues



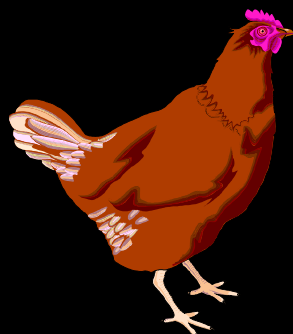
BSE to Pigs: Research



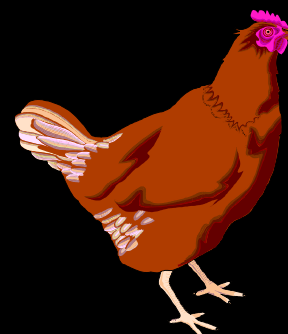


BSE to Chickens: Research

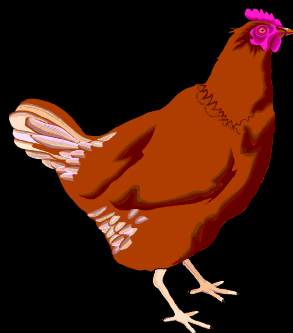
parenteral



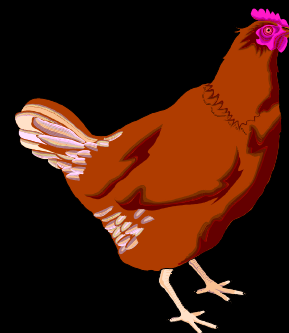
BSE

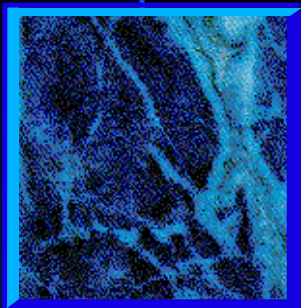


oral



BSE





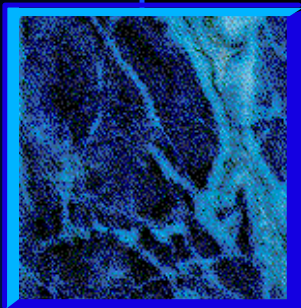
TSEs: Iatrogenic Transmission

■ Human TSEs

- ▲ dura mater grafts
- ▲ corneal transplants
- ▲ pituitary growth hormone
- ▲ EEG electrodes

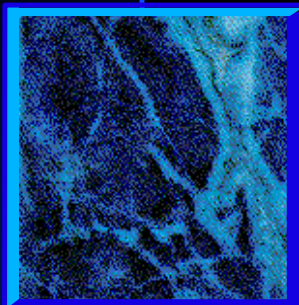
■ Scrapie

- ▲ Louping ill vaccine
- ▲ Mycoplasma agalactiae vaccine



BSE Diagnostics

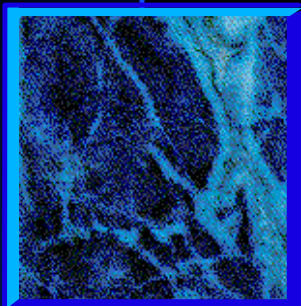
- No live animal test
- No preclinical test
- Need brain tissue
- Histology, IHC, WB, ELISA
- "Negatives" do not guarantee absence of infectivity



Diagnostics: Under Development

- Urine - UPrP_{sc}
(Gabizon et al., 2001)
- Increased sensitivity - cyclic amplification
(Soto et al., 2001)
- Cow-side test
- Capillary electrophoresis -

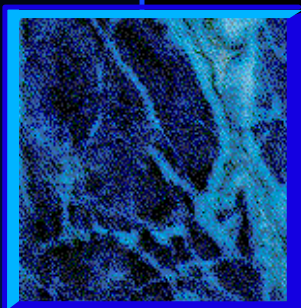




TSE Agents: Inactivation

- Sodium hypochlorite
20,000 ppm for 1 hour
- Sodium hydroxide
1 M at boiling temperatures - digester
- Wet heat, high temperatures

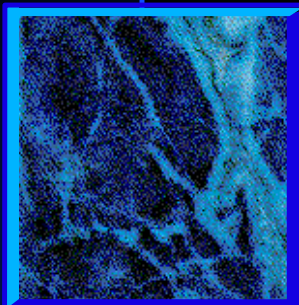




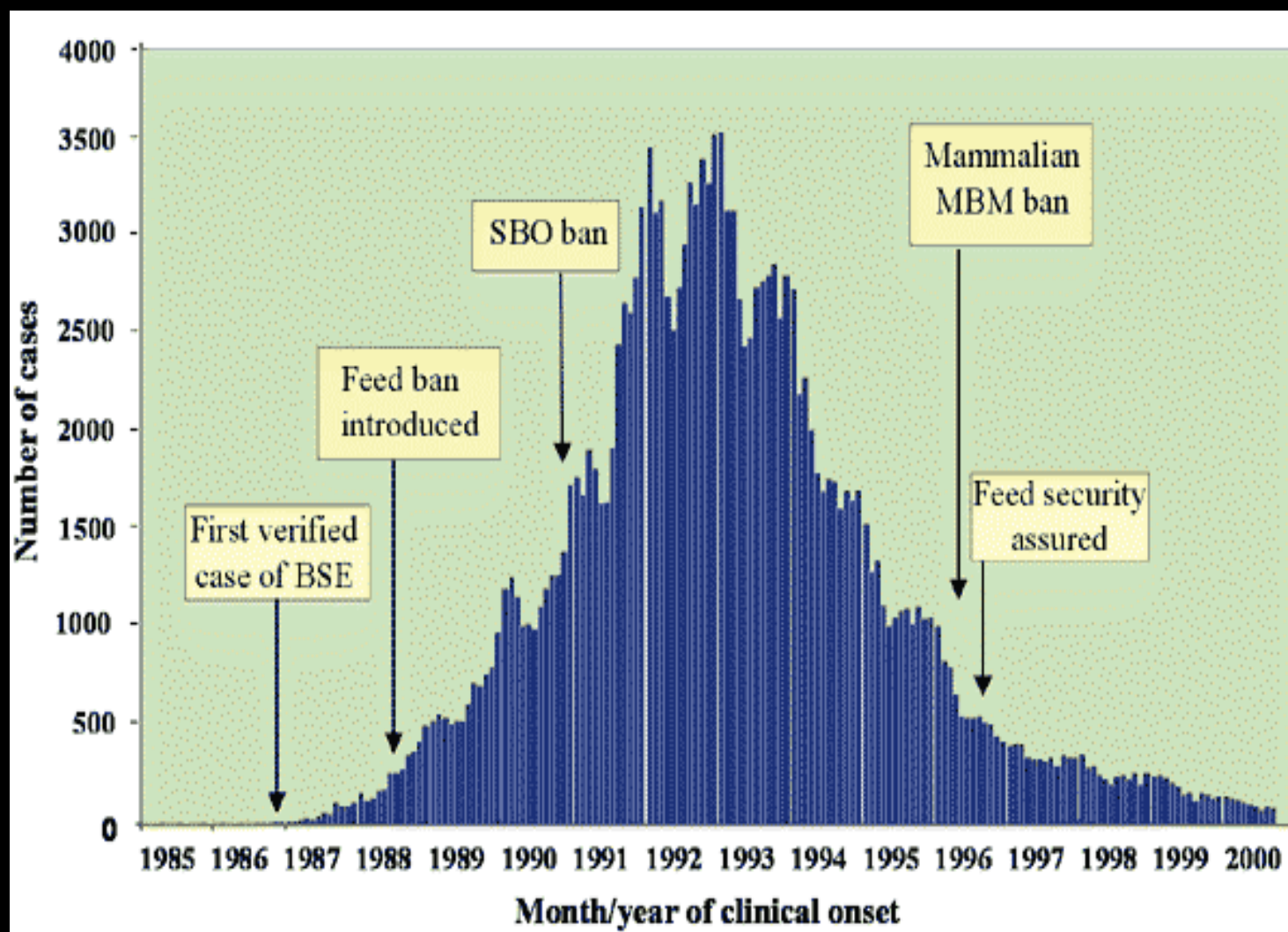
BSE STATISTICS for GREAT BRITAIN* (as of November 9, 2001)

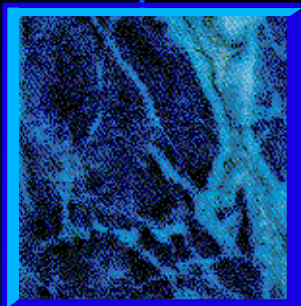
Total number of confirmed cases:	178,484
Total number of affected herds:	35,283
Proportion of dairy herds affected:	61.4%
Proportion of beef suckler herds affected:	16.7%
Confirmed total herd incidence:	37.6%

* England, Scotland, Wales



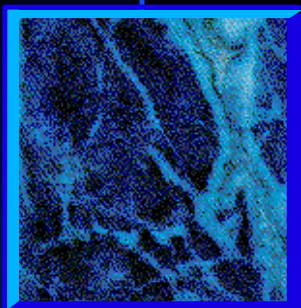
UK BSE Epidemic



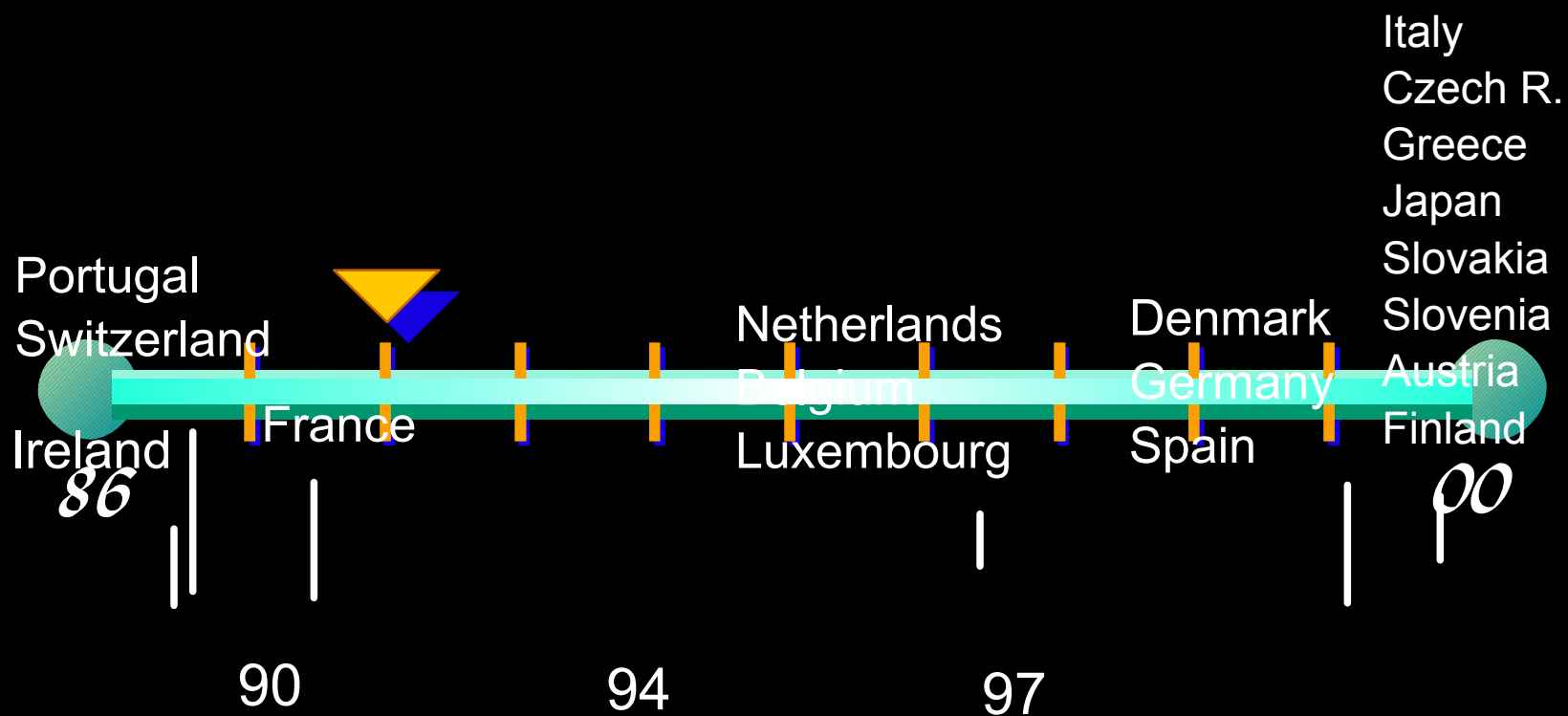


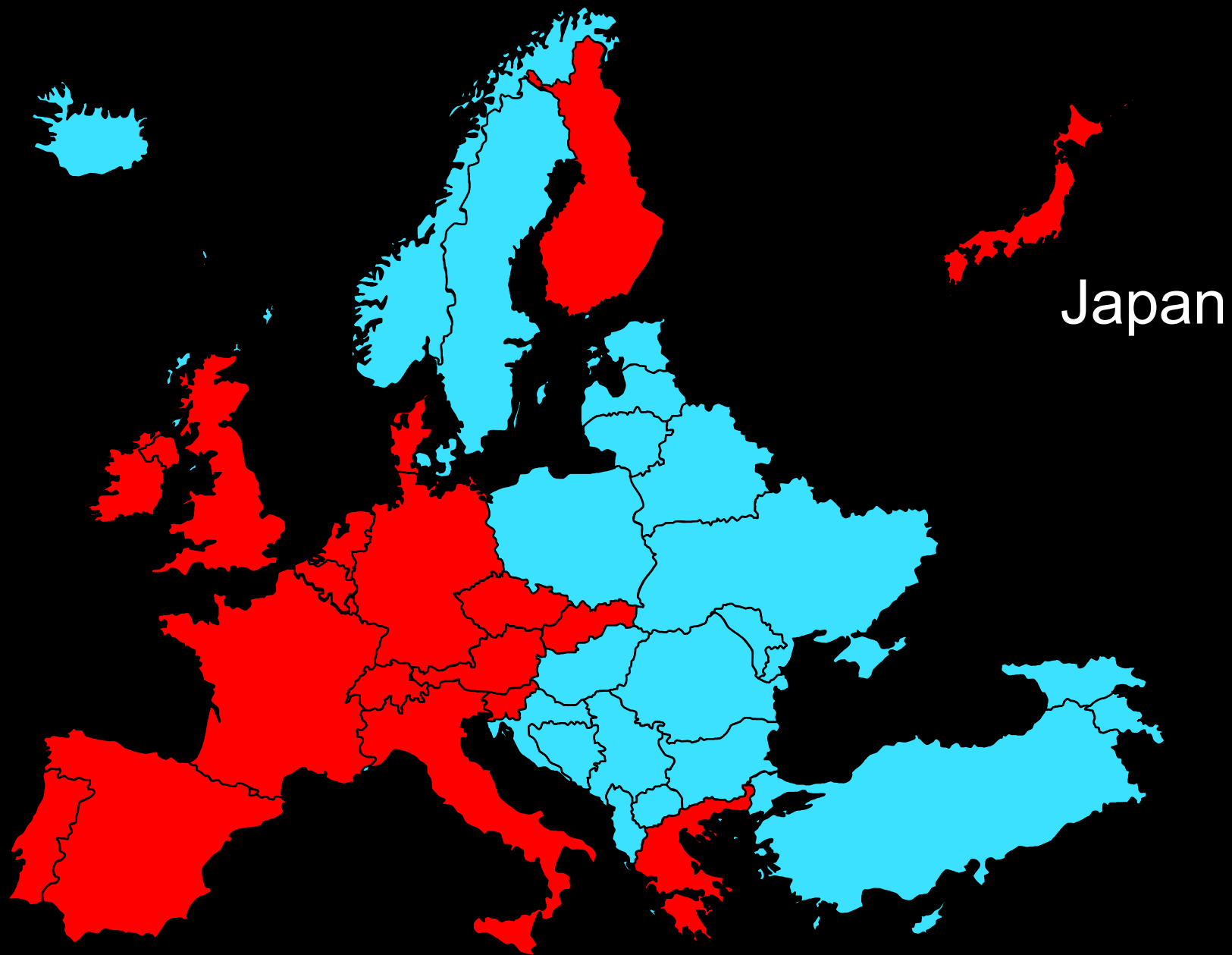
UK MAFF Actions

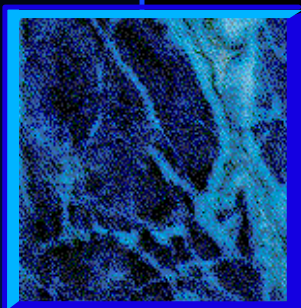
- Mammalian to food animal feed ban
- Over thirty month scheme
- Selective Cull
- Offspring Cull
- SRM/SBO bans
- Beef on the bone prohibition - No longer in place



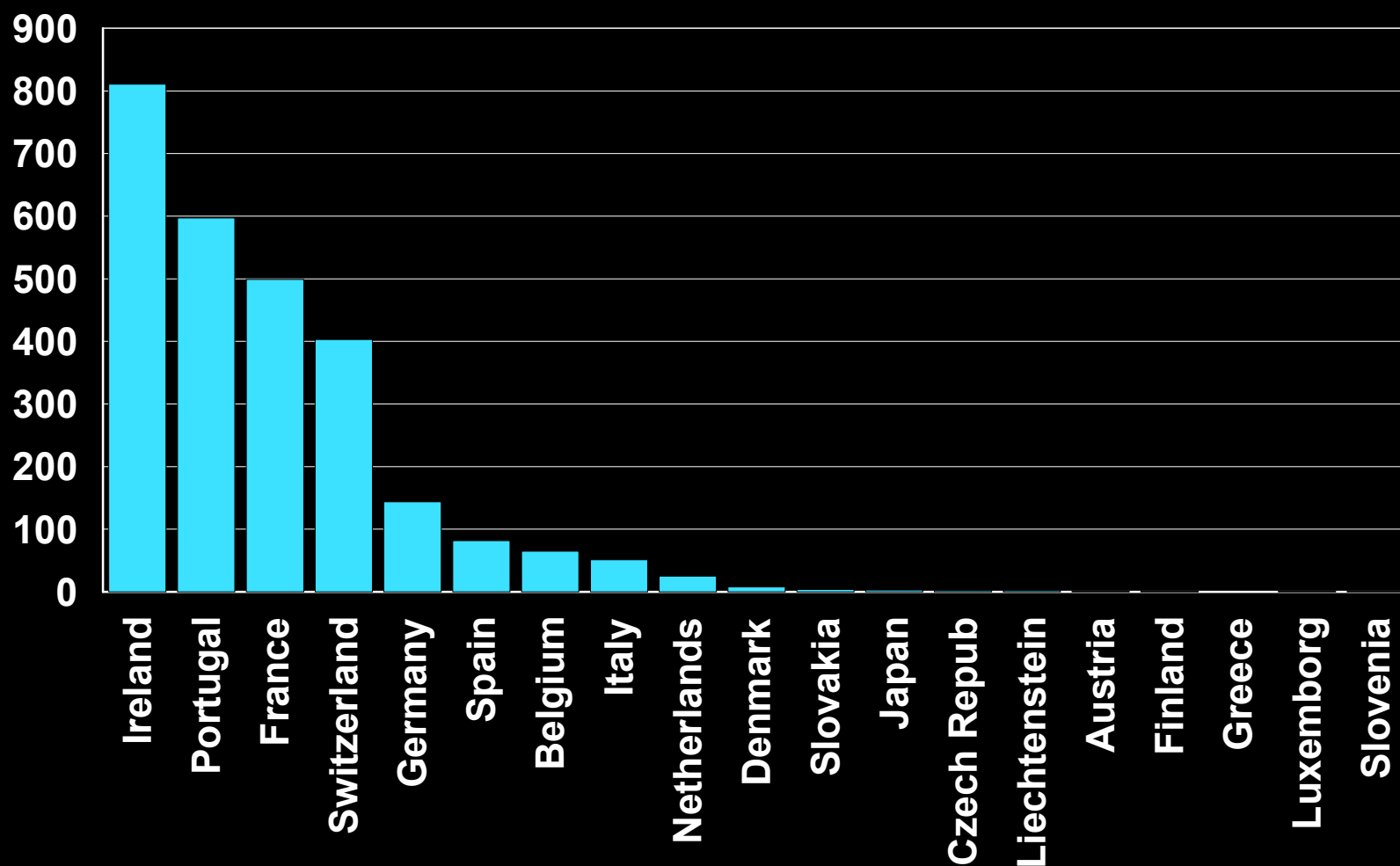
First cases of BSE

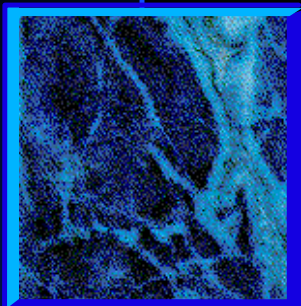






BSE Cases throughout the World

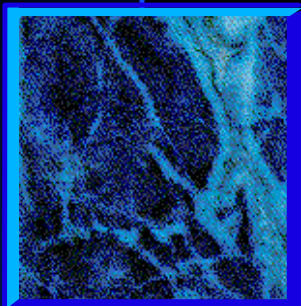




USDA ACTIONS: Prevention and Surveillance

- Import Regulations
- Surveillance
- Formal Risk Assessments
- TSE Working Group





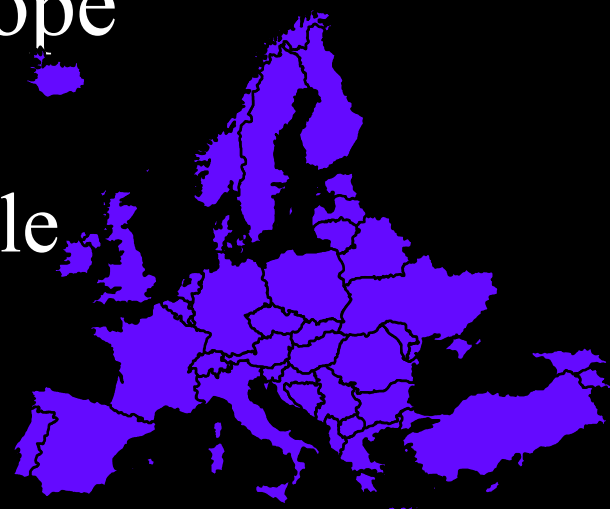
BSE - Prevention

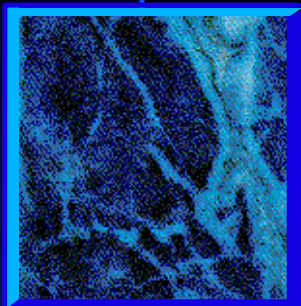
■ Import Restrictions - countries with BSE

- ▲ July 1989 - live ruminants
- ▲ November 1989 - ruminant products
- ▲ 1991 - formal regulations

■ Import Restrictions - Europe

- ▲ December 1997
- ▲ January 1998 - interim rule
- ▲ all live ruminants and most ruminant products





BSE - Prevention

■ Import Restrictions - Europe

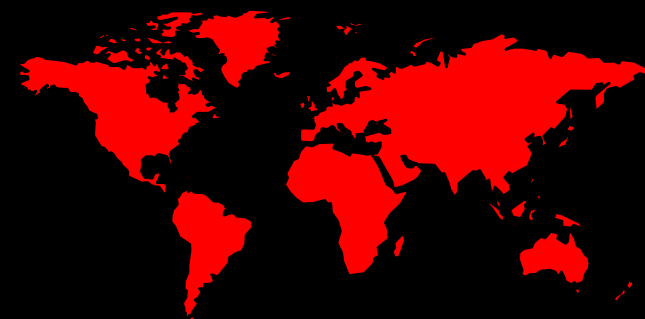
▲ December 6, 2000 - all MBM, etc.
regardless of species

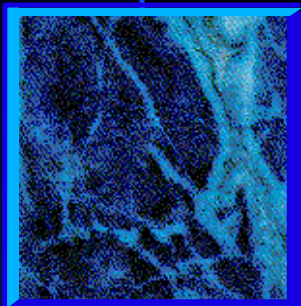
■ Evaluations of other countries

▲ South America underway

▲ Central America

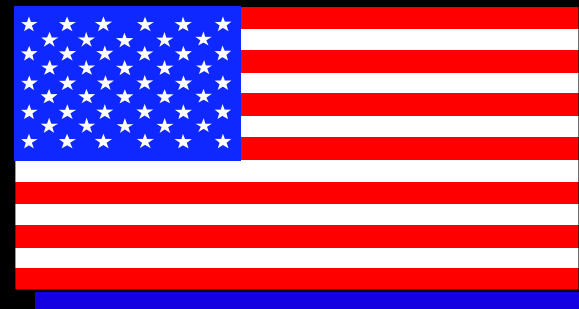
▲ Asia

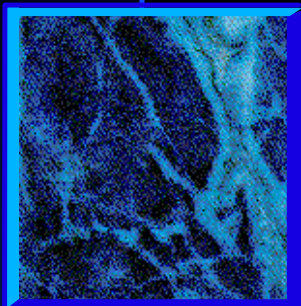




Import Policies and Regulations

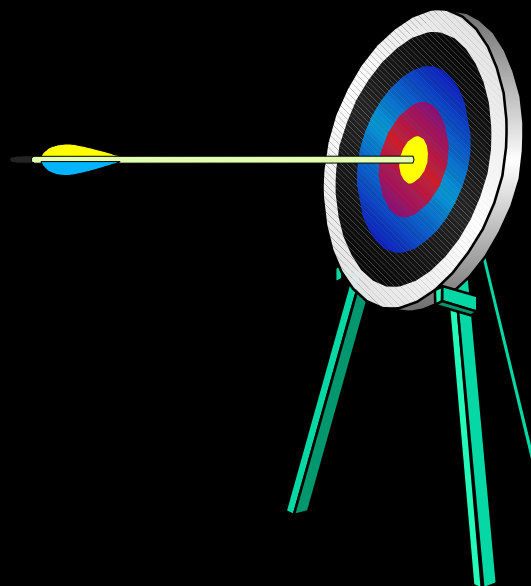
■ North American
Policy

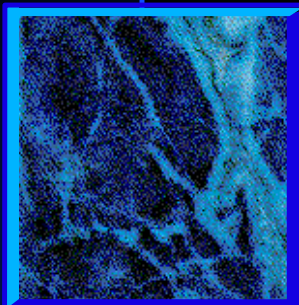




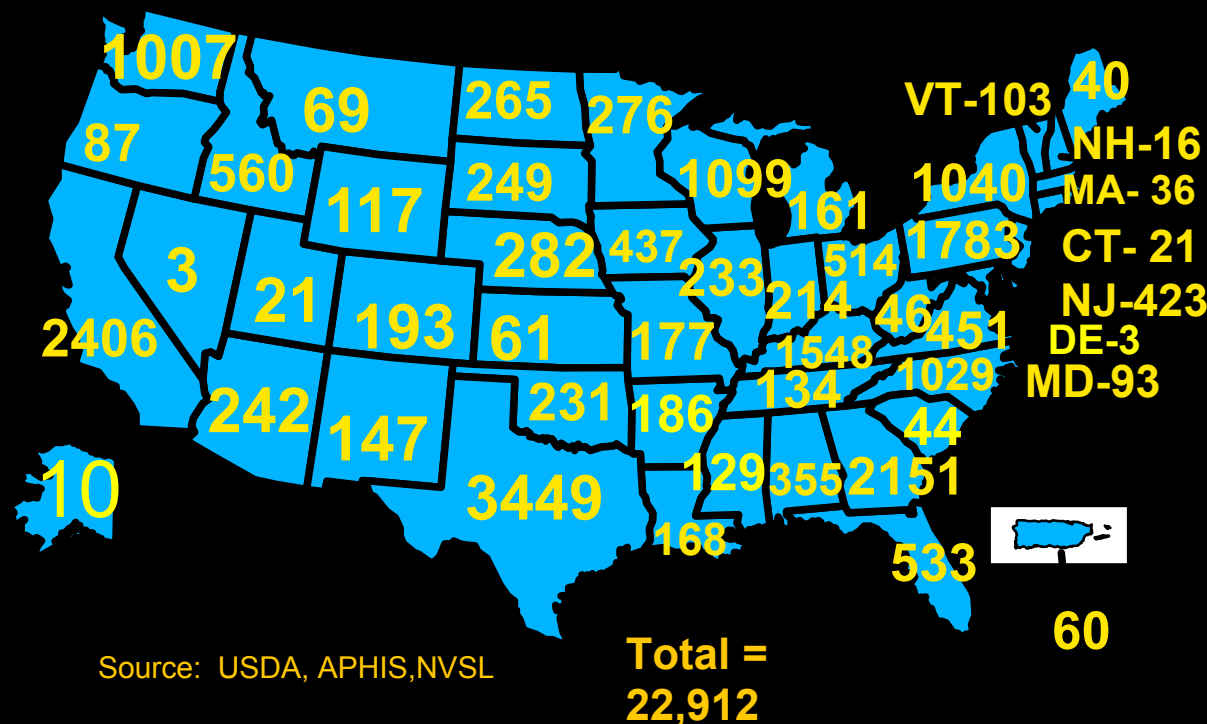
USDA ACTIONS: Surveillance

- CNS Cases - farms, labs, slaughter
- "Downers" - nonambulatory, fallen stock
- Deads from farms

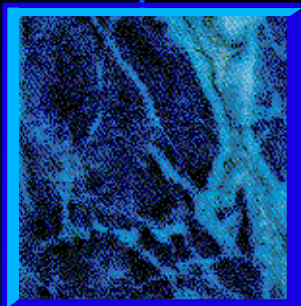




BSE Surveillance: Total Bovine Brain Submission by State May 10, 1990 thru February 28, 2002

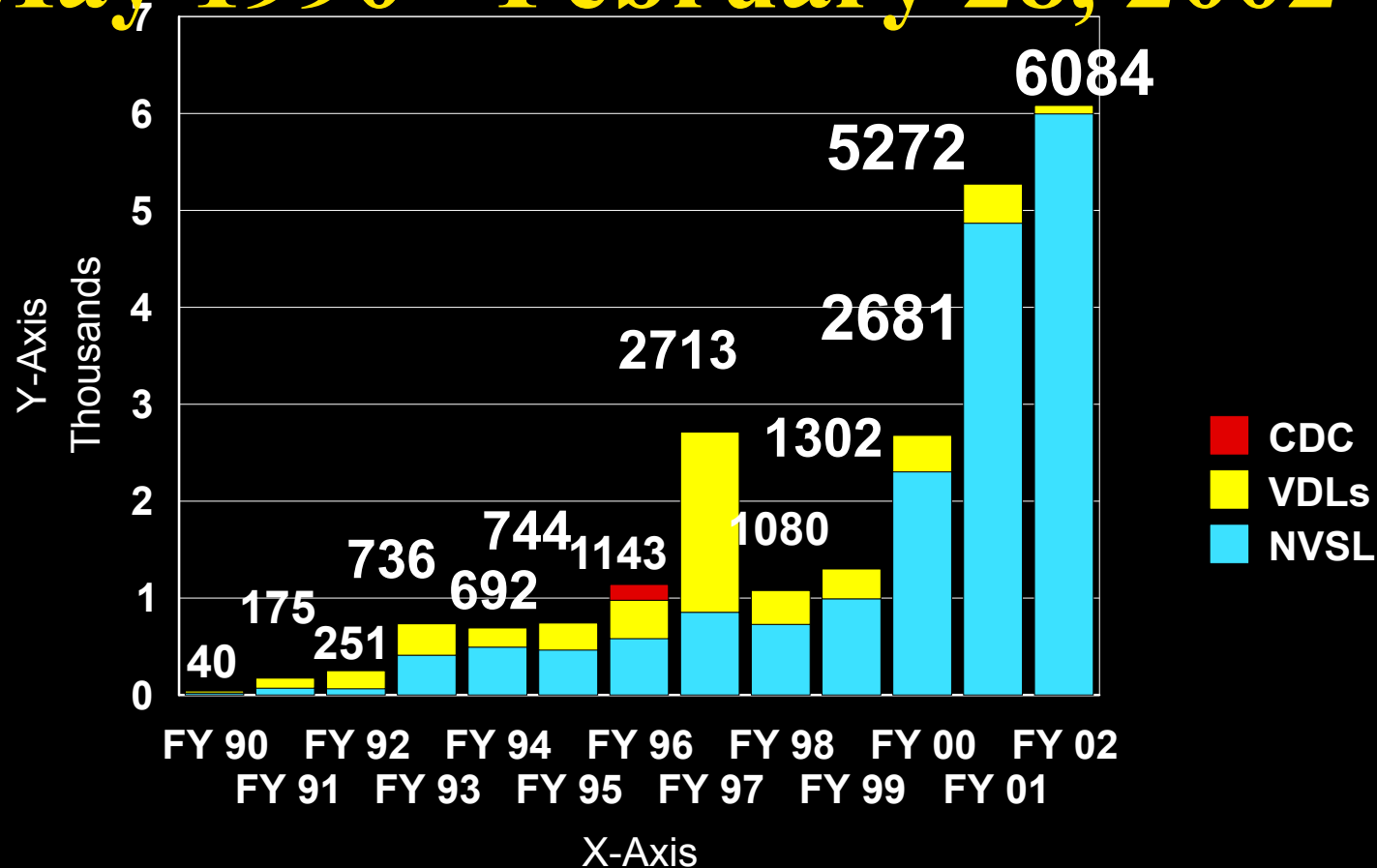


**No evidence of BSE
detected**

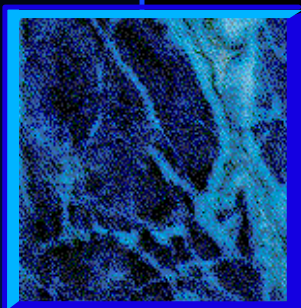


BSE Surveillance - Yearly Totals

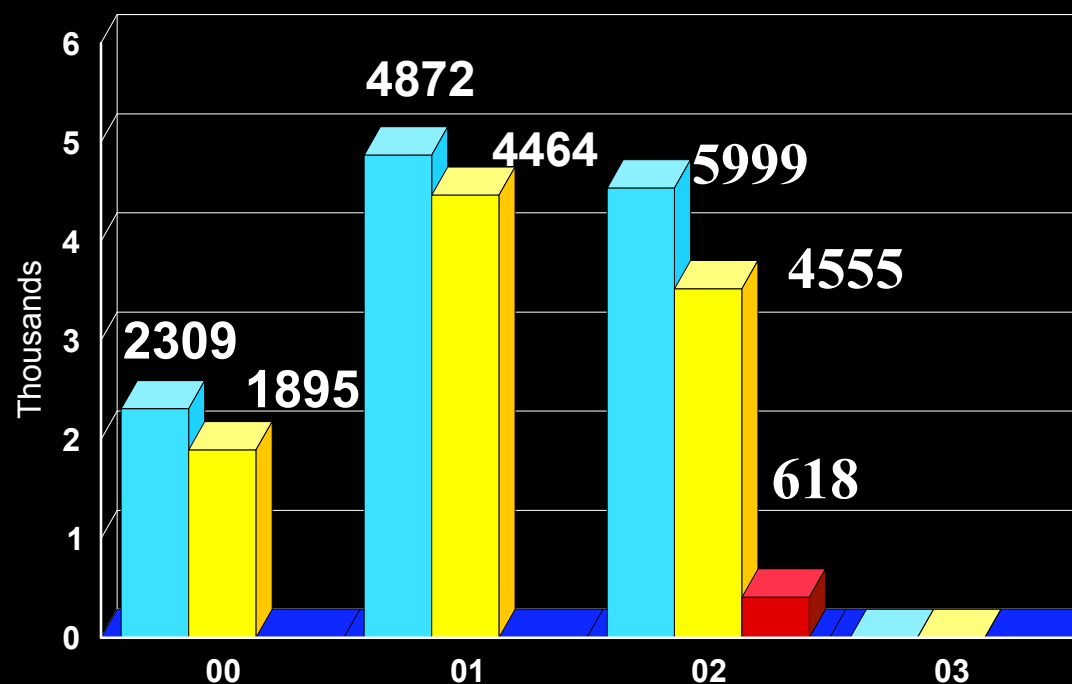
May 1990 - February 28, 2002



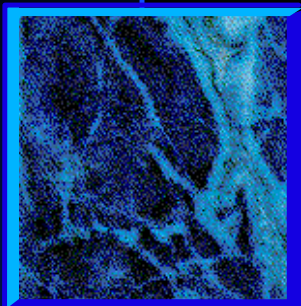
**No evidence of BSE
detected**



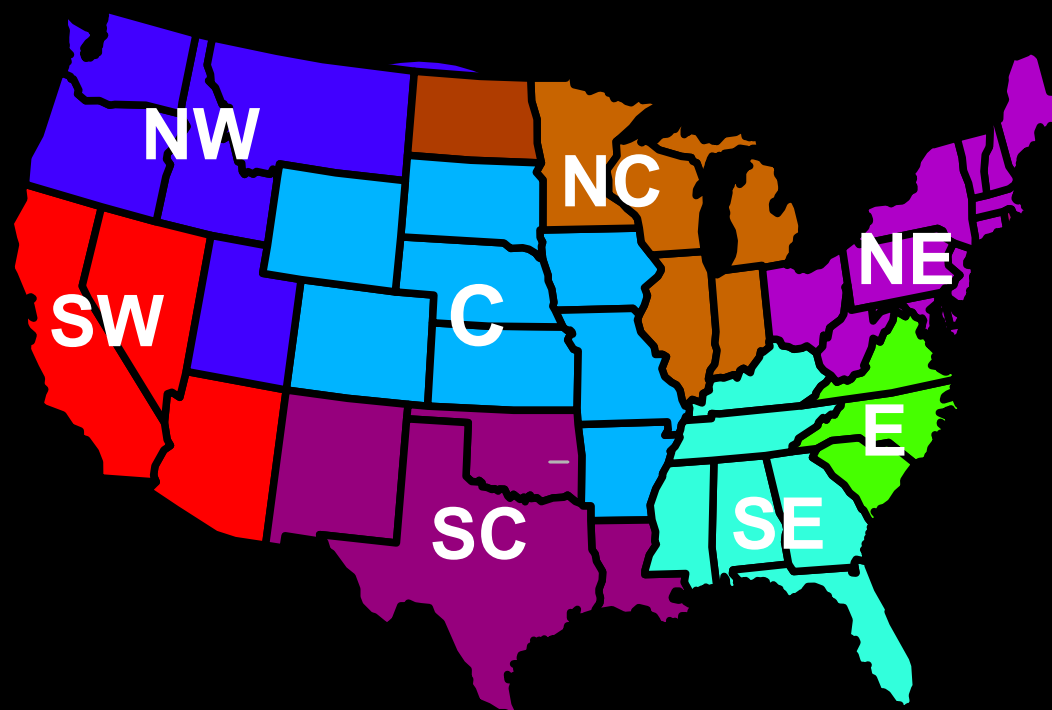
NVSL BSE Surveillance Bovine Brain Submissions FY 00-01 (as of 2-28-02)

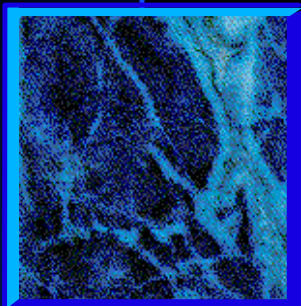


- Total Submissions
- "Downers" (fallen stock)
- Deaths from farms

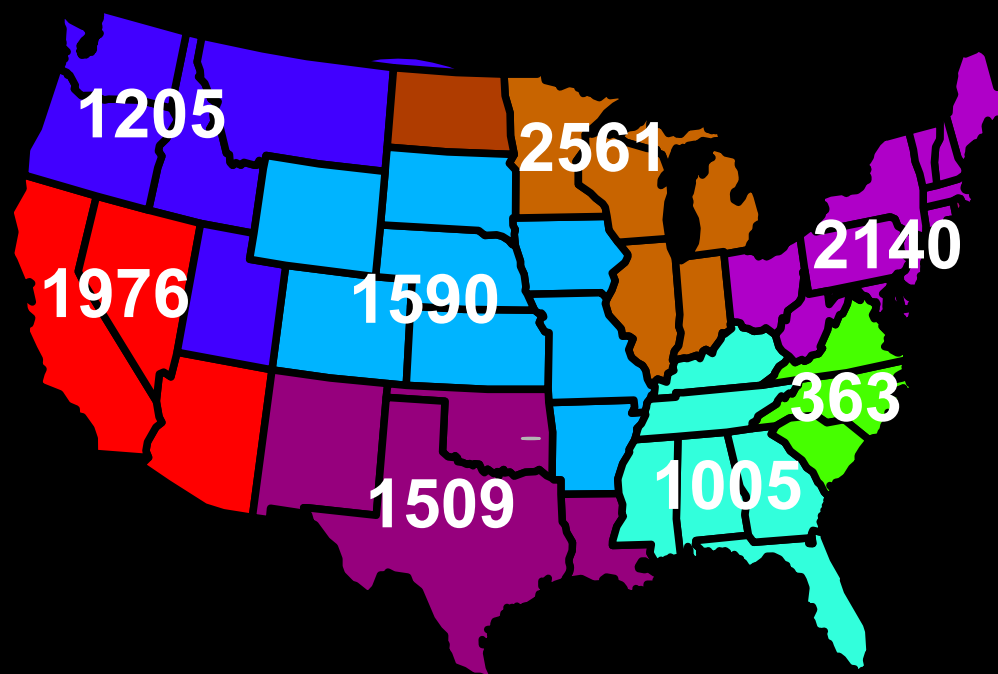


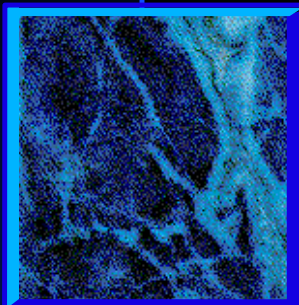
US Regions for BSE Surveillance





US Regional Goals for BSE Surveillance - FY 2002



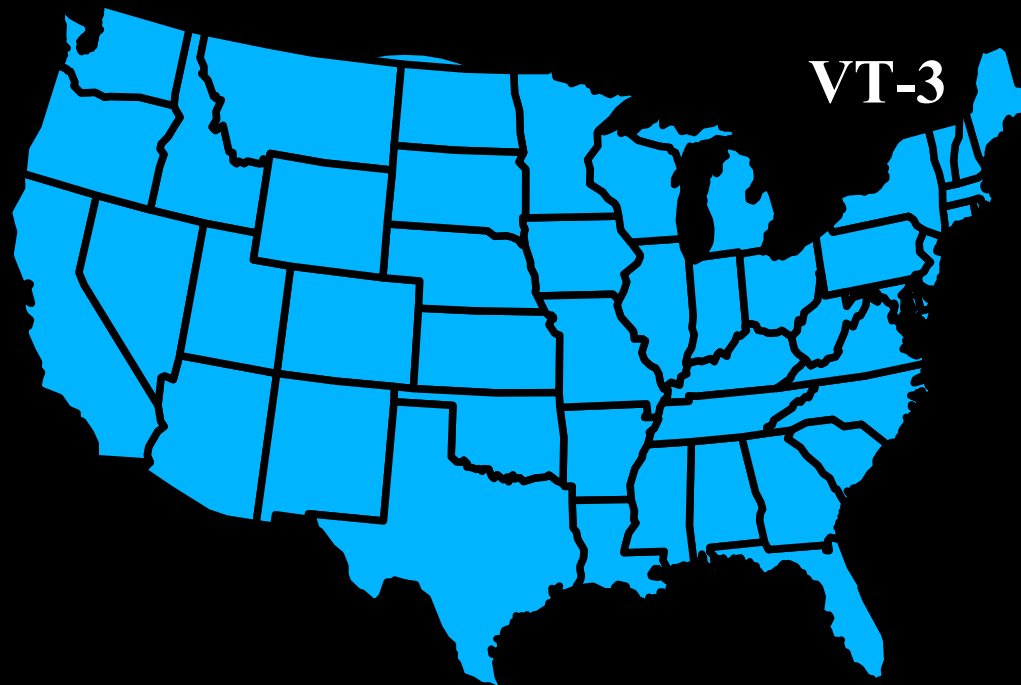
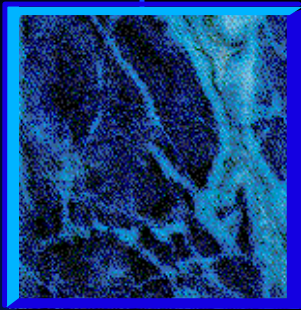


US Regional Goals for BSE Surveillance

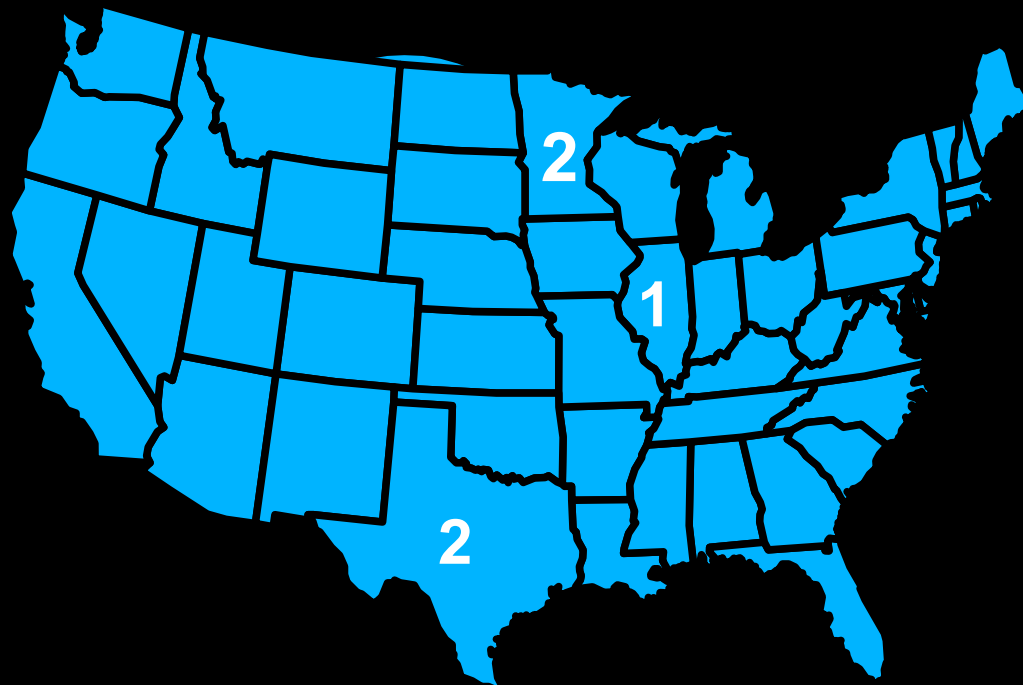
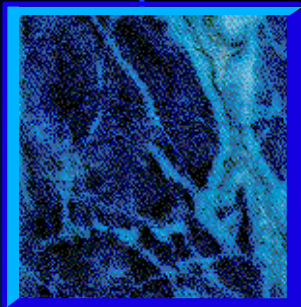
REGION	Goal FY 01	FY 01	Goal FY 02	FY 02
NW	564	695	1205	698
SW	466	564	1976	397
C	766	332	1590	245
SC	734	872	1509	822
NC	606	620	2561	491
NE	462	805	2140	983
E	312	401	363	790
SE	644	953	1005	1671

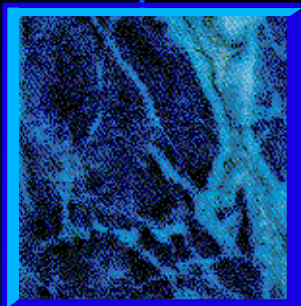
* as of February 28, 2002

Status of Cattle Imported into the US from the United Kingdom and Ireland (as of March 8, 2002)



Status of Cattle Imported into the US from other European countries in 1996-97 (as of March 8, 2002)





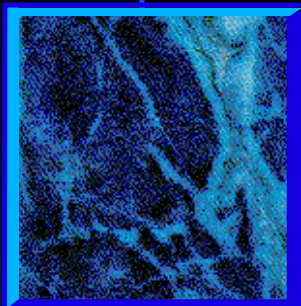
BSE Risk Assessment



Harvard School of
Public Health

Tuskegee University

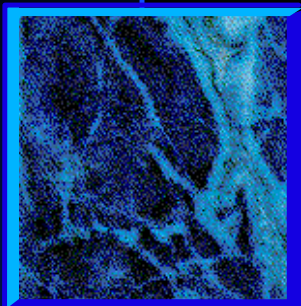
1998 -November
2001



Results

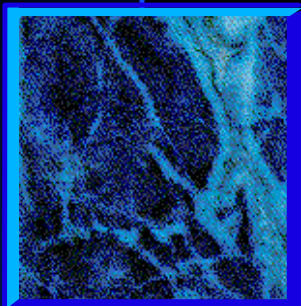
- US highly resistant to introduction of BSE and subsequent spread
- Spread within cattle herd mostly due to "leaks" in feed ban
- Potential human exposure through consumption of brain and spinal cord, AMR





USDA Requested

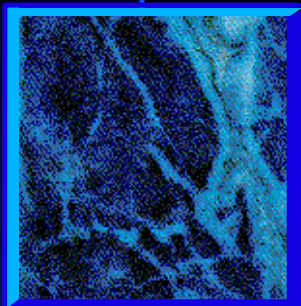
- Identify and characterize possible sources for BSE infectivity in U.S. cattle - **ie. WHERE MAY BSE COME FROM**
- Identify and characterize pathways for cattle-derived BSE infectivity in the U.S. cattle herd or human food supply - **HOW MAY BSE BE INTRODUCED TO US CATTLE OR PUBLIC**
- Evaluate implications over time of possible introduction of BSE into US system



Results (*continued*)

- Potential recycling within animal chain from deads off farms

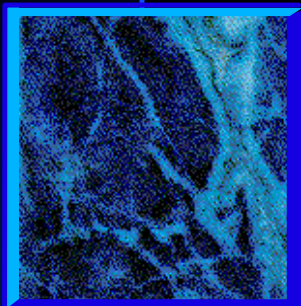




USDA's Response

- Increase surveillance
- Options to reduce human exposure
 - ▲ SRM ban
 - ▲ Pneumatic stunning
 - ▲ Restrictions on AMR
- Deads from farms - ANPR





CONCLUSIONS

- No BSE in US to date
- Continue conservative approach
- Continue and increase surveillance
- Adjust as science and policy dictates

